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Application Number	10553532
Filing Date	2005-10-14
First Named Inventor	Mark S. Cushman et al.
Art Unit	1625
Examiner Name	Aulakh
Attorney Docket Number	3220-78751

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CA	1	ANTONY et al., "Differential Induction of Topoisomerase I-DNA Cleavage Complexes by the Indenoisoquinoline MJ-III-65 (NSC 706744) and Camptothecin: Base Sequence Analysis and Activity Against Camptothecin-Resistant Topoisomerase I," Cancer Res., 2003, Vol. 63, pgs. 7428-7435	<input type="checkbox"/>
CA	2	ANTONY et al., "Cellular Topoisomerase I Inhibition and Antiproliferative Activity by MJ-III-65 (NSC 706744), an Indenoisoquinoline Topoisomerase I Poison," Molecular Pharmacology, 2005, Vol. 67, No. 2, 523-530	<input type="checkbox"/>
CA	3	CANAN KOCH et al., "Enantioselective Preparation of B-Alkyl-γ-butyrolactones from Functionalized Ketene Dithioacetals," J. Org. Chem., 1993, Vol. 58, No. 10, 2725-2737	<input type="checkbox"/>
CA	4	COREY et al., "A Total Synthesis of Natural 20(S)-Camptothecin," J. Org. Chem., Vol. 40, No. 14, 1975, pp. 2140-2141	<input type="checkbox"/>
CA	5	CUSHMAN et al., "Stereoselective Oxidation by Thionyl Chloride Leading to the Indeno[1,2-c]isoquinoline System," J. Org. Chem., 1978, Vol. 43, No. 19, pgs. 3781-3783	<input type="checkbox"/>
CA	6	CUSHMAN et al., "Synthesis and Antitumor Activity of Structural Analogues of the Anticancer Benzophenanthridine Alkaloid Fagaronine Chloride," J. Med. Chem., 1985, Vol. 28, No. 8, pp. 1031-1036	<input type="checkbox"/>

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CA	7	CUSHMAN et al., "Synthesis and Biological Activity of Structural Analogues of the Anticancer Benzophenanthridine Alkaloid Nitidine Chloride," J. Med. Chem., 1984, Vol. 27, No. 4, 544-547	<input type="checkbox"/>
CA	8	CUSHMAN et al., "Synthesis of New Indeno[1,2-c]isoquinolines: Cytotoxic Non-Camptothecin Topoisomerase I Inhibitors," J. Med. Chem., 2000, Vol. 43, No. 20, pgs. 3688-3698	<input type="checkbox"/>
CA	9	CUSHMAN et al., "Total Synthesis of Nitidine Chloride," J. Org. Chem., 1978, Vol. 43, No. 2, pgs. 286-288	<input type="checkbox"/>
CA	10	HERTZBERG et al., "On the Mechanism of Topoisomerase I Inhibition by Camptothecin: Evidence for Binding to an Enzyme-DNA Complex," Biochemistry, 1989, Vol. 28, No. 11, 4629-4638	<input type="checkbox"/>
CA	11	HERTZBERG et al., "Modification of the Hydroxy Lactone Ring of Camptothecin: Inhibition of Mammalian Topoisomerase I and biological Activity," J. Med. Chem., 1989, Vol. 32, No. 3, 715-720	<input type="checkbox"/>
CA	12	IOANOVICIU et al., "Synthesis and Mechanism of Action Studies of a Series of Norindenoisoquinoline Topoisomerase I Poisons Reveal an Inhibitor with a Flipped Orientation in the Ternary DNA-Enzyme-Inhibitor Complex As Determined by X-ray Crystallographic Analysis," J. Med. Chem., 2005, Vol. 48, No. 15, 4803-4814	<input type="checkbox"/>
CA	13	JAYARAMAN et al., "Novel Oxidative Transformation of Indenoisoquinolines to Isoquinoline-3-spiro-3'-phthalides in the Presence of Osmium Tetraoxide and 4-methylmorpholine N-Oxide," J. Org. Chem., 1998, Vol. 63, No. 17, 5736-5737	<input type="checkbox"/>
CA	14	JAYARAMAN et al., "Synthesis of New Dihydroindeno[1,2-c]isoquinoline and Indenoisoquinolinium Chloride Topoisomerase I Inhibitors Having High In Vivo Anticancer Activity in the Hollow Fiber Animal Model," J. Med. Chem., 2002, Vol. 45, No. 1, pgs. 242-249	<input type="checkbox"/>
CA	15	KOHLHAGEN et al., "Protein-Linked DNA Strand Breaks Induced by NSC 314622, a Novel Noncamptothecin Topoisomerase I Poison," Mol. Pharmacol., 1998, Vol. 54, pgs. 50-58	<input type="checkbox"/>
CA	16	KUBOVA et al., "Binding Properties of Nitidine and Its Indenoisoquinoline Analogue with DNA," Studia Biophys., 1986, Vol. 114, No. 1-3, pgs. 251-256	<input type="checkbox"/>
CA	17	LI et al., "Synthesis of the Tricyclic ABC Ring Subunit of Mazamine A," Tetrahedron, Vol. 54 (1998), 6661-6676	<input type="checkbox"/>

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CA	18	MORRELL et al., "Synthesis of nitrated indenoisoquinolines as topoisomerase I inhibitors," Bioorganic & Medicinal Chemistry Letters, Vol. 14 (2004), 3659-3663	<input type="checkbox"/>
CA	19	NAGARAJAN et al., "Design, Synthesis, and Biological Evaluation of Indenoisoquinoline Topoisomerase I Inhibitors Featuring Polyamine Side Chains on the Lactam Nitrogen," J. Med. Chem., 2003, Vol. 46, No. 26, pgs. 5712-5724	<input type="checkbox"/>
CA	20	NAGARAJAN et al., "Synthesis and Anticancer Activity of Simplified Indenoisoquinoline Topoisomerase I Inhibitors Lacking Substituents on the Aromatic Rings," J. Med. Chem., 2004, Vol. 47, No. 23, pgs. 5651-5661	<input type="checkbox"/>
CA	21	PATEL et al., "Neuromuscular blocking activity of bis-4-benzyltetrahydroisoquinolinium esters in the cat," European Journal of Pharmaceutical Sciences, Vol. 4 (1996), 63-71	<input type="checkbox"/>
CA	22	POMMIER et al, Editorial Overview " Topoisomerase Inhibitors: Why New Ones?", Opinion in Oncologic, Endocrine & Metabolic Investigational Drugs, 1(2), 168-169 (1999)	<input type="checkbox"/>
CA	23	POMMIER et al., "Mechanism and action of eukaryotic DNA topoisomerase I and drugs targeted to the enzyme," Biochem. Biophys. Acta., 1400, 83-106 (1998)	<input type="checkbox"/>
CA	24	POURQUIER et al., "Induction of Reversible Complexes between Eukaryotic DNA Topoisomerase I and DNA-containing Oxidative Base Damages," The Journal of Biological Chemistry, Vol. 274, No. 13, 1999, pp. 8516-8523	<input type="checkbox"/>
CA	25	SHETTY et al., "Aromatic -Stacking in Solution as Revealed through the Aggregation of Phenylacetylene Macrocycles," J. Am. Chem. Soc., 1996, Vol. 118, No. 5, pgs. 1019-1027	<input type="checkbox"/>
CA	26	SOMEKAWA et al., "Intramolecular [2+2]Photocycloadditions of 1-(w-Alkenyl)-2-pyridones Possessing an Ester Group on the Olefinic Carbon Chain," J. Org. Chem., 1992, Vol. 57, No. 21, 5708-5712	<input type="checkbox"/>
CA	27	STAKER et al., "Structures of Three Classes of Anticancer Agents Bound to the Human Topoisomerase I-DNA Covalent Complex," J. Med. Chem., 2005, Vol. 48, No. 7, 2336-2345.	<input type="checkbox"/>
CA	28	STAKER et al., "The Mechanism of Topoisomerase I Poisoning by a Camptothecin Analog," Proc. Natl. Acad. Sci. U. S.A., 2002, Vol. 99, No. 24, pgs. 15387-15392	<input type="checkbox"/>

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CA	29	STRUMBERG et al., "Synthesis of Cytotoxic Indenoisoquinoline Topoisomerase I Poisons," J. Med. Chem., 1999, Vol. 42, No.3, pgs. 446-457	<input type="checkbox"/>
CA	30	VANCE et al., "Structural Features of Nitroaromatics That Determine Mutagenic Activity in Salmonella typhimurium," Environmental Mutagenesis, 1984, Vol. 6, pgs. 797-811	<input type="checkbox"/>
CA	31	WANG et al., "Differential Effects of Camptothecin Derivatives on Topoisomerase I-Mediated DNA Structure Modification," Biochemistry, 1998, Vol. 37, No. 26, 9399-9408	<input type="checkbox"/>
CA	32	WANG et al., "Role of the 20-Hydroxyl Group in Camptothecin Binding by the Topoisomerase I-DNA Binary Complex," Biochemistry, 1999, Vol. 38, No. 14, 4374-4381	<input type="checkbox"/>
CA	33	WAWZONEK et al., "The Synthesis and Reactions of 1-Carbamyl-11-ketoindeno[1,2-c]isoquinoline," J. Org. Chem., 1966, Vol. 31, pp. 1004-1006	<input type="checkbox"/>
CA	34	WHITMORE et al., "The Preparation of Homophthalyl Cyclic Hydrazide and 4-Aminohomophthalyl Cyclic Hydrazide," J. Am. Chem. Soc., 1944, Vol. 66, pgs. 1237-1240	<input type="checkbox"/>
CA	35	XIAO et al., "Design, synthesis, and biological evaluation of cytotoxic 11-aminoalkenylindenoisoquinoline and 11-diaminoalkenylindenoisoquinoline topoisomerase I inhibitors," Bioorganic & Medicinal Chemistry, Vol. 12 (2004), 5147-5160	<input type="checkbox"/>
CA	36	XIAO et al., "Dihydroindenoisoquinolines function as prodrugs of indenoisoquinolines," Bioorganic & Medicinal Chemistry Letters, Vol. 15 (2005), 2795-2798	<input type="checkbox"/>
CA	37	XIAO et al., "Novel Autoxidative Cleavage Reaction of 9-Fluorenes Discovered during Synthesis of a Potential DNA-Threading Indenoisoquinoline," J. Org. Chem., 2004, Vol. 69, No. 22, 7495-7501	<input type="checkbox"/>
CA	38	XIAO et al., "On the Binding of Indeno[1,2-c]isoquinolines in the DNA-Topoisomerase I Cleavage Complex," J. Med. Chem., 2005, Vol. 48, No. 9, 3231-3238	<input type="checkbox"/>
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CA	AB	WO 01/30753 A2	05/03/2001	WO			xxx (In English)
	AC						
	AD						
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OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)							
CA	AH	CHO, Won-Jea et al., "A Novel Synthesis of Benzo[c]phenanthridine Skeleton and Biological Evaluation of Isoquinoline Derivatives," Chem. Pharm. Bull. Vol. 47, No. 6, 1999, pp. 900-902					
CA	AI	DYKE, S. F. et al., "The Chemistry of Cryptopine-I," Tetrahedron, Vol. 24, No. 3, 1968, pp. 1455-1465					
CA	AJ	FOX, Brian M. et al., "Design, Synthesis, and Biological Evaluation of Cytotoxic 11-Alkenylindenoisoquinoline Topoisomerase I Inhibitors and Indenoisoquinoline-Camptothecin Hybrids, J. Med. Chem., Vol. 46, No. 15, July 2003, pp. 3275-3282					
CA	AK	SHAMMA, M. et al., "Synthetic Approaches to Camptothecin," Tetrahedron, Vol. 25, No. 11, 1969, pp. 2275-2279					
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